78. The method of claim 51, wherein said cell is a human cell.

79. The method of claim 51, wherein said cell is a cell line.

80. The method of claim 51, wherein said cell is from liver tissue.

81. The cell of claim 51, wherein said cell is from gastrointestinal tract tissue.

82. The cell of claim 51, wherein said cell is from lung tissue.

83. The cell of claim 51, wherein said cell is from kidney tissue.--

REMARKS

THE AMENDMENTS AND REASONS FOR AMENDMENTS

Applicant cancels claims 1 through 20, and adds new claims 21 through 83, which correspond generally to canceled claims 1 through 20. These new claims add no new subject matter and are fully supported throughout the specification. Reference to gastrointestinal tract tissue is supported, for example at Page 2, Lines 1, 9-12, and at Page 19, Lines 21-23. Reference to MDR1 is supported, for example, at Page 16, Lines 4-5, at Page 18, Lines 9-12, and at Page 28, Lines19-20. The new claims are supported throughout the specification particularly by claims 1-20 as originally filed. The amendments are made to clarify the claimed invention and to expedite the allowance of the present application. Applicant reserves the right to file later applications claiming the benefit of priority to the present application. For the convenience of the Examiner, a marked up copy of the new claims are provided as Attachment A.

THE CLAIMED INVENTION COMPLIES WITH 35 U.S.C. 112

The Examiner rejected claim 2 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner states that there is insufficient antecedent basis in Claim 1 to support the recitation of "said enzyme" in claim 2. To expedite the allowance of the application, Applicant has provided new claims 21-81 that correspond generally to previous claims 1-20 that address a typographical error. Applicant respectfully request that this rejection be withdrawn.

THE PRIOR ART FAILS TO ANTICIPATE THE CLAIMED INVENTION UNDER 35 U.S.C. 102 (e)

Applicant's claimed invention is novel over prior art prior to amendment. To expedite the allowance of the application, however, Applicant has amended one claim, however, no amendment relates to prior art rejections. Applicant does so without prejudice to pursuing the original claims in another application.

The Examiner rejected Claims 1, 3, 4, 9, 11, 14-20 under 35 U.S.C. 102(e) as being anticipated by Lohray et al. (U.S. Patent No. 6,054,453).

Lohray does not teach each and every element of Applicant's claimed invention. The claims, as filed, refer to a cell comprising a first and second nucleic acid molecules. The first nucleic acid molecule comprises a promoter or enhancer operable for a nucleic acid molecule encoding a protein involved in drug metabolism operably linked to a reporter gene. The second nucleic acid molecule encodes an intracellular receptor or a transcriptinal factor, which when bound with, associated with, or activated by a compound, can operably bind with, associate with, or activate the promoter or enhancer resulting in the expression of the reporter gene.

The Examiner alleges that Lohray teaches a cell comprising two plasmids or nucleic acid molecules. The Examiner alleges that the first nucleic acid molecule taught by Lohray encodes a ligand binding domain fused to DNA binding domain of Yeast transcription factor GAL4, which the Examiner alleges corresponds with the second nucleic acid molecule of the present invention.

The Examiner alleges that the second nucleic acid molecule taught by Lohray is a reporter plasmid harboring the luciferase gene driven by a GAL4 specific promoter, which the Examiner alleges corresponds with the first nucleic acid molecule of the present invention.

The Examiner also alleges that Lohray teaches that when the cell is contacted with a compound that induces expression of the protein involved in drug metabolism, the reporter gene is expressed. The Examiner further alleges that GAL4 is a protein involved in drug metabolism, and the test compound induces the Expression of GAL4, which in turn causes the expression of the reporter (luciferase).

Applicant respectfully disagrees and notes that GAL4 is not a protein involved in drug metabolism, rather it is involved in galactose metabolism (please see documents: Attachments B through Attachment G, which are briefly summarized herein). Attachment B is a published study directed to identification of sites bound by GAL4. The study shows GAL4 is a yeast trasncriptional factor that activates genes necessary for galactose metabolism. The study found 10 genes to be bound by GAL4, all of which were involved in galactose metabolism. Attachment C is an article about regulation of protein synthesis. This article describes in detail the role of GAL4 in regulation of genes that encode enzymes that carry out steps in galactose metabolism. Attachment D is an article about the complex interactions that connect genes to phenotypes. This article describes GAL4 as a regulator, the product of which increases the expression of all genes that code for enzymes that catalyze the transformation of galactose into glucose 6-phosphate. Attachment E is an article about functional genomics that describes a study that identified 3 previously unknown genes that are bound and upregulated by GAL4. The study described the new GAL4 targets as genes involved in sugar metabolism in yeast. Attachment F is a summary of a lecture about the function of GAL4 as a transcriptional factor for the galactose unitization genes. Attachment G is a list of proteins putatively regulated by the GAL4 protein. In contrast to galactose, the specification refers to drugs as xenobiotics, Page 14, Lines 28-28. Stedman's Medical Dictionary, 24th edition, describes a drug as "a therapeutic agent; any substance, other than food, used in the prevention, diagnosis, alleviation, treatment, or cure of diseases in man and animal." See Attachment H.

Secondly, Lohray teaches the testing of compounds to determine the activity of hPPAR Alpha (which mediates fatty acid oxidation, Column 2, Lines 35-36), which is not the expression of proteins involved in drug metabolism. Unlike Lohray, the cell of the present invention includes a nucleic acid molecule that encodes a protein involved in drug metabolism. Furthermore, the second nucleic acid molecule of the present invention encodes an intracellular receptor or a transcription factor. Lohray does not teach use of a nucleic acid molecule that encodes an intracellular receptor. Lohray teaches the use of a nucleic acid that encodes transcription factor that is a fusion two separate domains: a ligand binding domain fused with GAL4 DNA binding domain.

Accordingly, this reference does not anticipate the claimed invention by not teaching each and every element of the claimed invention. Applicant thus respectfully requests that this rejection be withdrawn.

APPLICANT'S CLAIMED INVENTION IS NOT OBVIOUS UNDER 35 U.S.C. § 103(A) IN VIEW OF THE REFERENCES CITED BY THE EXAMINER

Applicant's claimed invention is non-obvious over the prior art prior to amendment. To expedite the allowance of the application, however, Applicant has amended one claim, however no amendment related to prior art rejections. Applicant does so without prejudice to pursuing the original claims in another application.

1. The Examiner rejected Claim 2 under 35 U.S.C. 103(a) as being unpatentable over Lohray et al. in view of Lusky et al. (U.S. Patent No. 6,262,118).

The cited references, either alone or in combination, fail to render the claimed invention obvious. The Examiner alleges that Lusky teaches there were indications of drug-drug interactions of racemic halofenate with agents such as Coumadin, and the cytochrome P450 enzymes are likely to be involved in the metabolism of Coumadin. However, Lusky does not teach or suggest a cell comprising a first nucleic acid molecule comprising a promoter or

enhancer operable for a nucleic acid molecule encoding a protein involved in drug metabolism operably linked to a reporter gene, and a second nucleic acid molecule encoding an intracellular receptor or a transcription factor, which when bound with, associated with, or activated by a compound, can operably bind with, associate with, or activate the promoter or enhancer resulting in the expression of the reporter gene. As such, Luskey does not make up for the deficiencies of Lohray previously referred to, and thus, the combination fails to make the claimed invention obvious.

For the forgoing reasons, Applicant submits that the rejected claims cannot be obvious over the Lohray et al. and Luskey et al. references under 35 U.S.C. §103(a). Accordingly, Applicant respectfully requests that this rejection be withdrawn.

2. The Examiner rejected Claims 5-7 under 35 U.S.C. 103(a) as being unpatentable over Lohray et al. in view of Foulkes et al. (U.S. Patent No. 5,976,793).

The cited references, either alone or in combination, fail to render the claimed invention obvious. The Examiner alleges that Foulkes teaches a reporter gene that is inserted in the chromosome of the cell, downstream of, and under the control of an endogenous promoter. However, Foulkes does not teach or suggest a cell comprising a first nucleic acid molecule comprising a promoter or enhancer operable for a nucleic acid molecule encoding a protein involved in drug metabolism operably linked to a reporter gene, and a second nucleic acid molecule encoding an intracellular receptor or a transcriptinal factor, which when bound with, associated with, or activated by a compound, can operably bind with, associate with, or activate the promoter or enhancer resulting in the expression of the reporter gene. As such, Foulkes does not make up for the deficiencies of Lohray previously referred to, and thus the combination fails to make the claimed invention obvious. Furthermore, Claim 5 (new claim 25) states that the first nucleic acid of claim 1, which is made up of the promoter and reporter, is inserted within the chromosome of a cell, thus the inserted nucleic acid molecule made up of the promoter and reporter is not under the control of the endogenous promoter as taught by Foulkes.

For the forgoing reasons, Applicant submits that the rejected claims cannot be obvious over the Lohray et al. and Foulkes et al. references under 35 U.S.C. §103(a). Accordingly, Applicant respectfully requests that these rejections be withdrawn.

3. The Examiner rejected Claim 8 under 35 U.S.C. 103(a) as being unpatentable over Lohray et al. in view of Boeke et al. (U.S. Patent No. 5,840,579).

The cited references, either alone or in combination, fail to render the claimed invention obvious. The Examiner alleges that Boeke teaches the use of an endogenous reporter. However, Boeke does not teach or suggest a cell comprising a first nucleic acid molecule comprising a promoter or enhancer operable for a nucleic acid molecule encoding a protein involved in drug metabolism operably linked to a reporter gene, and a second nucleic acid molecule encoding an intracellular receptor or a transcription factor, which when bound with, associated with, or activated by a compound, can operably bind with, associate with, or activate the promoter or enhancer resulting in the expression of the reporter gene. As such, Boeke does not make up for the deficiencies of Lohray previously referred to, and thus the combination fails to make the claimed invention obvious.

For the forgoing reasons, Applicant submits that the rejected claims cannot be obvious over the Lohray et al. and Boeke et al. references under 35 U.S.C. §103(a). Accordingly, Applicant respectfully requests that this rejection be withdrawn.

4. The Examiner rejected Claim 10 under 35 U.S.C. 103(a) as being unpatentable over Lohray et al. in view of Klein et al. (U.S. Patent No. 6,255,959).

The cited references, either alone or in combination, fail to render the claimed invention obvious. The Examiner alleges that Klein teaches the use of orphan receptors. However, Klein does not teach or suggest a cell comprising a first nucleic acid molecule comprising a promoter or enhancer operable for a nucleic acid molecule encoding a protein involved in drug metabolism operably linked to a reporter gene, and a second nucleic acid molecule encoding an intracellular receptor or a transcription factor, which when bound with, associated with, or activated by a

compound, can operably bind with, associate with, or activate the promoter or enhancer resulting in the expression of the reporter gene. As such, Klein does not make up for the deficiencies of Lohray previously referred to, and thus the combination fails to make the claimed invention obvious.

For the forgoing reasons, Applicant submits that the rejected claims cannot be obvious over the Lohray et al. and Klein et al. references under 35 U.S.C. §103(a). Accordingly, Applicant respectfully requests that this rejection be withdrawn.

5. The Examiner rejected Claims 12 and 13 under 35 U.S.C. 103(a) as being unpatentable over Lohray et al. in view of Sherr et al. (U.S. Patent No. 6,303,722).

The cited references, either alone or in combination, fail to render the claimed invention obvious. The Examiner alleges that Sherr teaches the use of an endogenous transcription factor to activate selective transcription of a heterologous gene. However, Sherr does not teach or suggest a cell comprising a first nucleic acid molecule comprising a promoter or enhancer operable for a nucleic acid molecule encoding a protein involved in drug metabolism operably linked to a reporter gene, and a second nucleic acid molecule encoding an intracellular receptor or a transcription factor, which when bound with, associated with, or activated by a compound, can operably bind with, associate with, or activate the promoter or enhancer resulting in the expression of the reporter gene. As such, Sherr does not make up for the deficiencies of Lohray previously referred to, and thus the combination fails to make the claimed invention obvious.

For the forgoing reasons, Applicant submits that the rejected claims cannot be obvious over the Lohray et al. and Sherr et al. references under 35 U.S.C. §103(a). Accordingly, Applicant respectfully requests that these rejections be withdrawn.

Applicants respectfully submit that the claims are ready for examination and in condition for allowance.

Respectfully submitted,

Date: Oct 17, 2002

David R. Preston
Reg. No. 38,710

David R. Preston & Associates, A.P.C.
12625 High Bluff Drive, Suite 205
San Diego, CA 92130
Telephone: 858.724.0375
Facsimile: 858.724.0384

ATTACHMENT A

--[1.] 21. A cell, comprising:

a first nucleic acid molecule comprising:

a promoter or enhancer operable for a nucleic acid molecule encoding a protein involved in drug metabolism;

a reporter gene,

wherein said promoter or enhancer is operably linked to said reporter gene; and

a second nucleic acid encoding an intracellular receptor or transcription factor,

wherein when said intracellular receptor or transcription factor is bound with, associated with or activated by a compound, said intracellular receptor or transcription factor can operably bind with, associate with or activate said promoter or enhancer resulting in the expression of said reporter gene;

wherein when said cell is contacted with a compound that induces the expression of said protein involved in drug metabolism, said reporter gene is expressed.

[2.] 22. The cell of claim [1] 21, wherein said [enzyme] protein involved in drug metabolism is [selected from the group consisting of] a P450[s, glucuronosyl transferases, N-acetyltransferases, p-glyoproteins, glutathione transferases and sulfo transferases].

23. The cell of claim 21, wherein said protein involved in drug metabolism is a glucuronosyl trasferase.

24. The cell of claim 21, wherein said protein involved in drug metabolism is a N-acetyltransferase.

25. The cell of claim 21, wherein said protein involved in drug metabolism is a p-glycoprotein

26. The cell of claim 21, wherein said protein involved in drug metabolism is a glutothione transferase.

27. The cell of claim 21, wherein said protein involved in drug metabolism is a sulfo transferase.

28. The cell of claim 21, wherein said protein involved in drug metabolism is MDR1.

[3.] 29. The cell of claim [1] 21, wherein said reporter gene encodes an enzyme [or a detectable protein].

30. The cell of claim 21, wherein said reporter gene encodes a detectable protein.

[4.] 31. The cell of claim [1] 21, wherein said first nucleic acid molecule is present in an extrachromosomal element.

[5.] 32. The cell of claim [1] 21, wherein said first nucleic acid molecule is within the chromosome of said cell.

[6.] 33. The cell of claim [1] 21, wherein said reporter gene is inserted into the chromosome of said cell.

[7.] 34. The cell of claim [1] 21, wherein said enhancer or promoter is endogenous to the chromosome of said cell.

[8.] 35. The cell of claim [1] 21, wherein said reporter gene is endogenous to the chromosome of said cell.

[9.] 36. The cell of claim [1] 21, wherein said intracellular receptor or transcription factor forms a complex with a drug[, chemical or metabolite thereof] and directly or indirectly produces transcriptional activation of a gene encoding a protein involved in drug metabolism.

37. The cell of claim 21, wherein said intracellular receptor or transcription factor form a complex with a chemical and directly or indirectly prodeces transcriptional activation of a gene encoding a protein involved in drug metabolism.

38. The cell of claim 21, wherein said intracellular receptor or transcription factor forms a complex with a metabolite and directly or indirectly prodeces transcriptional activation of a gene encoding a protein involved in drug metabolism.

[10.] 39. The cell of claim [1] 21, wherein said intracellular receptor or transcription factor is an orphan receptor [or a hormone receptor].

40. The cell of claim 21, wherein said intracellular receptor or transcription factor is a hormone receptor.

[11.] 41. The cell of claim [1] 21, wherein said second nucleic acid molecule is present in an extrachromosomal element.

[12.] 42. The cell of claim [1] 21, wherein said second nucleic acid molecule is present within the chromosome of said cell.

[13.] 43. The cell of claim [1] 21, wherein said second nucleic acid molecule is endogenous to the chromosome of said cell.

[14.] 44. The cell of claim [1] 21, wherein said cell is a mammalian cell.

[15.] 45. The cell of claim [1] 21, wherein said cell is a transformed cell.

[16.] 46. The cell of claim [1] 21, wherein said cell is a human cell.

[17.] 47. The cell of claim [1] 21, wherein said cell is a cell line.

[18.] 48. The cell of claim [1] 21, wherein said cell is from [a] liver tissue [selected from the group consisting of liver, lung or kidney].

49. The cell of claim 21, wherein said cell is from gastrointestinal tract tissue.

50. The cell of claim 21, wherein said cell is from lung tissue.

51. The cell of claim 21, wherein said cell is from kidney tissue.

[19.] 52. A method for evaluating compounds for the property of inducing the expression of a gene encoding a protein involved in drug metabolism, comprising;

providing a test compound;

contacting said test compound with [the] a cell [of claim [1] 21], comprising:

a first nucleic acid molecule comprising:

a promoter or enhancer operable for a nucleic acid molecule encoding a protein involved in drug metabolism;

a reporter gene,

wherein said promoter or enhancer is operably linked to said reporter gene; and

a second nucleic acid encoding an intracellular receptor or transcription factor, wherein when said intracellular receptor or transcription factor is bound with, associated with or activated by a compound, said intracellular receptor or transcription factor can operably bind with, associate with or activate said promoter or enhancer resulting in the expression of said reporter gene;

wherein when said cell is contacted with a compound that induces the expression of said protein involved in drug metabolism, said reporter gene is expressed; and

detecting the expression of said reporter gene;

wherein expression of said reporter gene is indicative that said compound altered the expression of a gene encoding a protein involved in drug metabolism.

[20.] 53. The method of claim [19] 51, wherein said method is a high throughput method.

54. The method of claim 51, wherein said protein involved in drug metabolism is a P450.

55. The method of claim 51, wherein said protein involved in drug metabolism is a glucuronosyl transferase.

56. The method of claim 51, wherein said protein involved in drug metabolism is a N-acetyltrasferase.

57. The method of claim 51, wherein said protein involved in drug metabolism is a p-glycoprotein.

58. The method of claim 51, wherein said protein involved in drug metabolism is MDR1

59. The method of claim 51, wherein said protein involved in drug metabolism is a glutathione trasferase.

60. The method of claim 51, wherein said protein involved in drug metabolism is a sulfo transferase.

61. The method of claim 51, wherein said reporter gene encodes an enzyme.

62. The method of claim 51, wherein said reporter gene encodes a detectable protein.

63. The method of claim 51, wherein said first nucleic acid molecule is present in an extrachromosomal element.

64. The method of claim 51, wherein said first nucleic acid molecule is within the chromosome of said cell.

65. The method of claim 51, wherein said reporter gene is inserted into the chromosome of said cell.

66. The method of claim 51, wherein said enhancer or promoter is endogenous to the chromosome of said cell.

67. The method of claim 51, wherein said reporter gene is endogenous to the chromosome of said cell.

68. The method of claim 51, wherein said intracellular receptor or transcription factor forms a complex with a drug and directly or indirectly produces transcriptional activation of a gene encoding a protein involved in drug metabolism.

69. The method of claim 51, wherein said intracellular receptor or transcription factor forms a complex with a chemical and directly or indirectly produces transcriptional activation of a gene encoding protein involved in drug metabolism.

70. The method of claim 51, wherein said intracellular receptor or transcription factor forms a complex with a metabolite and directly or indirectly produces transcriptional activation of a gene encoding protein involved in drug metabolism.

71. The method of claim 51, wherein said intracellular receptor or transcription factor is an orphan receptor.

72. The method of claim 51, wherein said intracellular receptor or transcription factor is a hormone receptor.

73. The method of claim 51, wherein said second nucleic acid molecule is present in an extrachromosomal element.

74. The method of claim 51, wherein said second nucleic acid molecule is present within the chromosome of said cell.

75. The method of claim 51, wherein said second nucleic acid molecule is endogenous to the chromosome of said cell.

76. The method of claim 51, wherein said cell is a mammalian cell.

77. The method of claim 51, wherein said cell is a transformed cell.

78. The method of claim 51, wherein said cell is a human cell.

79. The method of claim 51, wherein said cell is a cell line.

80. The method of claim 51, wherein said cell is from liver tissue .

81. The cell of claim 51, wherein said cell is from gastrointestinal tract tissue.

82. The cell of claim 51, wherein said cell is from lung tissue.

83. The cell of claim 51, wherein said cell is from kidney tissue.--

ATTACHMENT B